UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,749	07/11/2001	Avi Ashkenazi	10466/43	5380

35489 7590 06/20/2005

HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
CHERNYSHEV, OLGA N	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,749	ASHKENAZI ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *39-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *39-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims and Response to Arguments

1. Claims 39-43 are pending in the instant application. Claims 39-43 are under examination in the instant office action.

2. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed on May 06, 2005 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 102

5. Claims 39-43 stand rejected under 35 U.S.C. 102(a) as being anticipated by WO99/58660 for those reasons of record in previous office communications. Briefly, because the effective filing date of the instant application is awarded as 2/22/2000, WO99/58660 document is considered to be 102(a) art.

The distinguishing property of the instant invention, antibodies that bind to the polypeptide of SEQ ID NO: 2, is established based on the disclosed utility of the polypeptide of SEQ ID NO: 2, which is useful for inhibition of VEGF stimulated proliferation of adrenal cortical capillary endothelial cells, which was disclosed in application filed on 2/22/2000. It has been further concluded that the instant specification fails to provide any scientific reasoning or factual evidence to support the assertion of the use of the polypeptide of SEQ ID NO: 2 as a

diagnostic marker for lung and colon cancer tumors. Therefore, if the polypeptide of SEQ ID NO: 2 does not have a substantial or well-established utility as a diagnostic marker, subsequently, an antibody that binds the polypeptide of SEQ ID NO: 2 also lacks specific and substantial or well-established utility as a biomarker. Because antibodies to polypeptide of SEQ ID NO: 2 lack specific and substantial credible utility as cancer markers, one skilled in the art clearly would not know how to use the claimed invention. 35 U.S.C. 120 or 119(e) makes it clear that in order to claim priority to the prior application (the parent or original nonprovisional application or provisional application), the disclosure of the invention in the prior application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See MPEP 201.11. Therefore, because the earlier application filed on 10 September 1998 does not comply with the requirements of the first paragraph of 35 U.S.C. 112 for failure to provide an adequate enablement on how to use the instant claimed antibodies as cancer markers, the instant application is granted the priority date of 02/22/2000.

Applicant traverses the rejection by addressing the issues related to the asserted utility of the clamed antibodies as markers for lung and colon cancer. At pages 3-5 of the Response, Applicant reviews the Utility Examination Guidelines, case law pertained to utility and appropriate sections of MPEP. Applicant's review of the issue of utility, the case law that has been cited and the holding that is found in that case law is not disputed. The only point of disagreement appears to be the interpretation of what constitutes a specific, substantial and credible utility.

At page 6 of the Response, Applicant submits that "[t]able 8 explicitly states that PRO211 is significantly overexpressed in lung and colon tumors as compared to the normal

control. [...] The above disclosure is sufficient to establish a specific, substantial and credible utility for the PRO211 polypeptide and its antibodies". The Examiner maintains the position that gene amplification of polynucleotides encoding PRO211 of SEQ ID NO: 2 in primary samples of lung and colon cancer, as indicated in Table 9 on pages 230-234 of the instant specification, is not predictive of increased amounts of polypeptide of SEQ ID NO: 2, and, therefore, the polypeptide of SEQ ID NO: 2 could not be used as a marker for lung and colon cancer without further and significant amount of experimentation.

Applicant refers to publications of Ortnoft et al., Hayman et al. and Pollack et al. to support the position that proteins expressed by genes that are amplified in tumors can be used as markers for cancer and states that "it is more likely than not" that a gene which is amplified in tumor cells will have increased gene expression" (top at page 8 of the Response). Applicant's arguments have been fully considered but are not persuasive for the following reasons.

The full analysis of the publications submitted with the reply filed on October 15, 2004, was presented in the previous office action of record. To summarize, publications of Orntoft et al., Hayman et al. and Pollack et al. (1) are mostly limited to the analysis of correlation between increased copy of DNA and corresponding amount of mRNA, which is not relevant in the instant case to support the correlation between DNA and protein levels; (2) explain that cases when copy of DNA is amplified less than 2-fold, which is only 3 out of 13 cases of lung cancer samples and zero out of 6 cases of colon cancer samples in the instant case of polypeptide of SEQ ID NO: 2 (see Table 9), are considered "at the border of detection" (page 43, second column and also page 37, top of the second column of Orntoft et al. paper); (3) clearly caution regarding limitations of gene expression pattern analysis, "[d]espite this progress in diagnostic

classification, the molecular mechanisms underlying gene expression patterns in cancer have remained elusive, and the utility of gene expression profiling in the identification of specific therapeutic targets remained limited" (Hayman et al., page 6240, first column).

Regarding the merit of the argument, even if to assume that the increase of DNA copy correlates with the increase of the amount of corresponding protein, there appears to be no evidence or scientific reasoning presented to conclude that such increase is directly proportional to the amount of number of copies of DNA, the only information available from the instant specification, as filed. Applicant submits that "it is not a legal requirement to establish a "necessary" correlation between an increase in the copy number of the mRNA and protein expression levels that would correlate to the disease state or that it is "imperative" to find evidence that protein levels can be accurately predicted" (middle at page 11 of the Response). However, in view of total absence of the biological significance of the polypeptide of SEQ ID NO: 2 in lung and colon cancer, recognition of "a positive correlation" between marginally overexpressed DNA in a limited number of lung and colon cancer tissue samples is only suitable for further research to establish if and what amount of the polypeptide of SEQ ID NO: 2 is diagnostic for what type of lung or colon cancer. It is a matter of law that the claimed invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention.

Applicant's asserted utility for the polypeptide of SEQ ID NO: 2, particularly in view of lack of knowledge as to the biological function of the polypeptide of SEQ ID NO: 2 with respect to lung or colon cancer, the type of cancer which can be diagnosed, and how much of the polypeptide of SEQ ID NO: is indicative of disease, constitutes a utility that requires further

research to identify or reasonably confirm a "real world" context of use. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966). This type of utility is not considered a "substantial utility". Furthermore, if the polypeptide of SQE ID NO: 2 does not have a substantial or well-established utility as a diagnostic cancer marker or as a therapeutic target, it is unclear as to what is the specific and substantial or well-established utility of an antibody that bind to a polypeptide which lacks that utility. Thus, for the reasons set forth, the claimed antibodies do not have a real-world use within the context of utility as markers for lung and colon cancer. As such, the instant application was not enabled for the use of the claimed antibodies as cancer markers as of filing date of September 1998. Therefore, the instant rejection under 102(a) is maintained.

Conclusion

6. No claim is allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (571) 273-0870. Official papers should NOT be faxed to (571) 273-0870.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1646

June 14, 2005